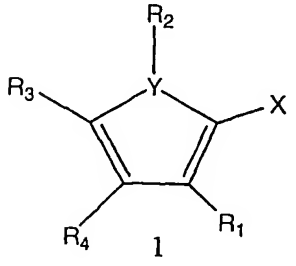
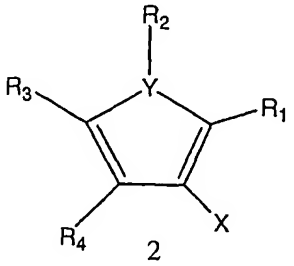
What is claimed is:

1. A compound that inhibits base exchange more than deacetylation by a SIR2 enzyme, in a pharmaceutically acceptable excipient, wherein the compound is selected from the group consisting of Formula I, Formula II, Formula III, Formula IV, and Formula V, wherein Formula I has one of Structures 1-8:



1



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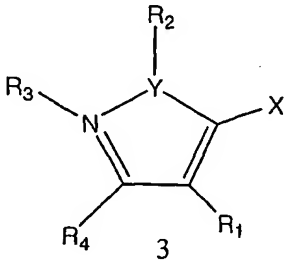

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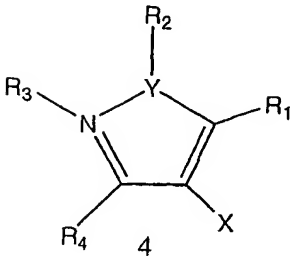

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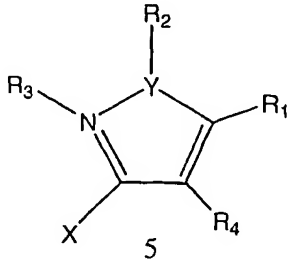

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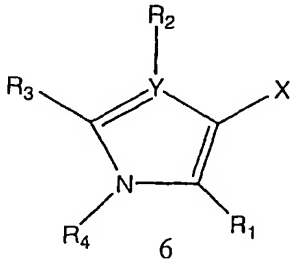

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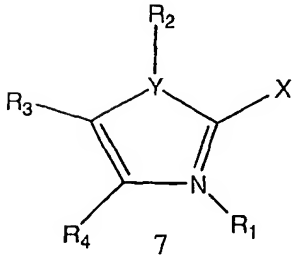
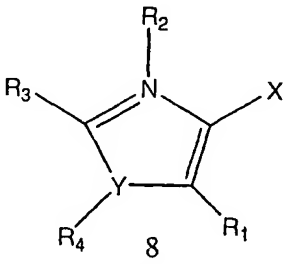


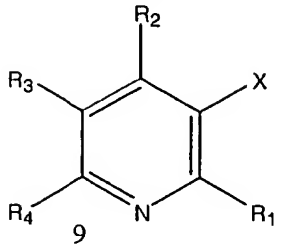
7



8

wherein $R_1$, $R_2$, $R_3$ and $R_4$ are independently H, F, Cl, Me, OH, $NH_2$, $CF_3$ or Me; X is CONHMe, $COCH_3$, $COCH_2CH_3$, $COCF_3$, $CH_2OH$ or $CH_2NH_2$; and Y is N, O, or S; when Y = S or O, the corresponding R is not defined;

Formula II has one of Structures 9-18:



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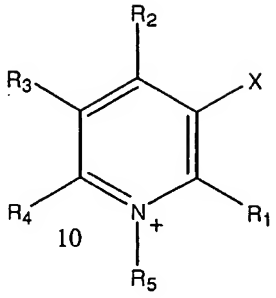
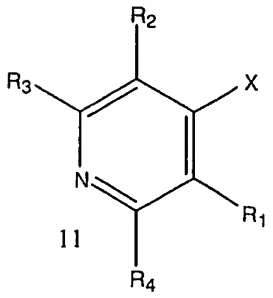


10



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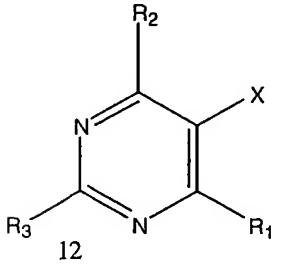

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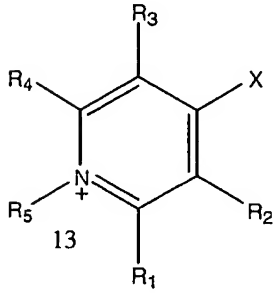

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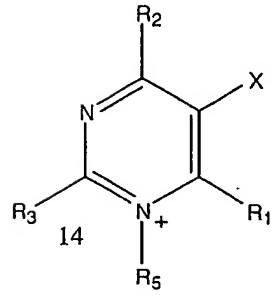

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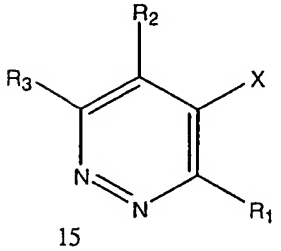

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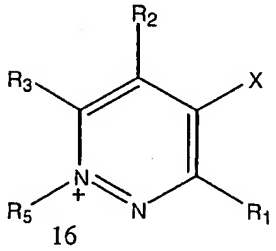
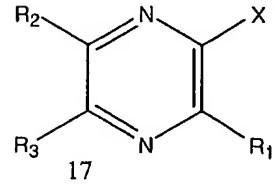
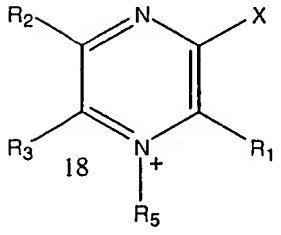


16



17

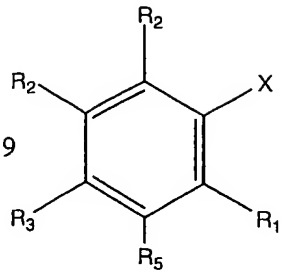


18

wherein $R_1$, $R_2$, $R_3$ and $R_4$ are independently H, F, Cl, OH, $NH_2$, Me or $CF_3$; X is $CONH_2$, CONHMe, $COCH_3$, $COCH_2CH_3$, $COCF_3$, $CH_2OH$ or $CH_2NH_2$; and $R_5$ is Me, $CF_3$, O or $NH_2$, and wherein Formula II is not nicotinamide;

Formula III has one of Structures 19 or 20:

19



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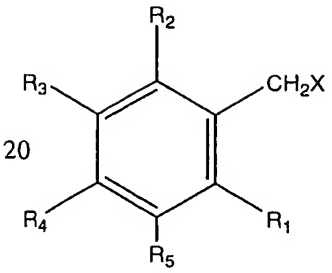
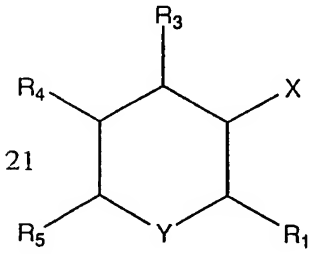


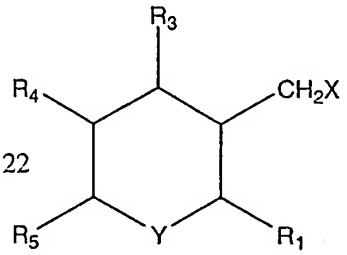
wherein $R_1$, $R_2$, $R_3$, $R_4$, and $R_5$ are independently H, F, Cl, OH, $NH_2$, Me or $CF_3$; and X is $CONH_2$, CONHMe, $COCH_3$, $COCH_2CH_3$, $COCF_3$, $CH_2OH$ or $CH_2NH_2$;

Formula IV has one of Structures 21 or 22:

21



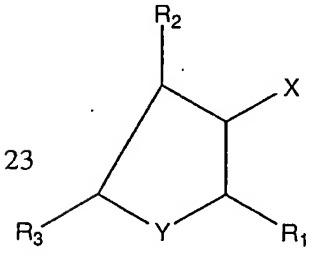
22



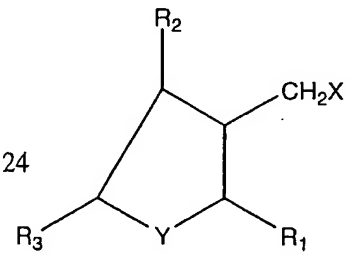
wherein the ring may comprise zero, one or two double bonds; $R_1$, $R_2$, $R_3$, and $R_4$ are independently H, F, Cl, OH, $NH_2$, Me or $CF_3$; and X is $CONH_2$, CONHMe, $COCH_3$, $COCH_2CH_3$, $COCF_3$, $CH_2OH$ or $CH_2NH_2$; and Y is N, O or S; and

Formula V has one of Structures 23 or 24:

23



24



wherein the ring may comprise zero or one double bond; $R_1$, $R_2$, and $R_3$ are independently H, F, Cl, OH, $NH_2$, Me or $CF_3$; and X is $CONH_2$, CONHMe, $COCH_3$, $COCH_2CH_3$, $COCF_3$, $CH_2OH$ or $CH_2NH_2$; and Y is N, O or S.

2. The compound of claim 1, wherein the compound has Formula I.

3. The compound of claim 1, wherein the compound has Formula II.

4. The compound of claim 1, wherein the compound has Formula III.

5. The compound of claim 1, wherein the compound has Formula IV.

6. The compound of claim 1, wherein the compound has Formula V.

7. The compound of claim 1, wherein the compound is selected from the group consisting of Structures 1, 2, 6, 21, 22, 23 and 24, where X is $CONH_2$ and Y is N; Structure 9, where at least one of $R_1$-$R_4$ is F and X is $CONH_2$; Structure 11, where $R_1$, $R_2$, $R_3$ and $R_4$ are independently H or F and X is $CONH_2$; and Structures 19 and 20, where at least one of $R_1$-$R_5$ is F and X is $CONH_2$.

8. The compound of claim 1, wherein the compound is selected from the group consisting of Structure 1 and 2, where $R_2$ is $CH_3$, and $R_1$, $R_3$ and $R_4$ is H; Structure 6, where $R_1$, $R_3$ and $R_4$ is H and $R_2$ is $CH_3$ or H; Structure 9, where $R_1$ is F, $R_2$-$R_4$ is H, and X is $CONH_2$ (2-fluoronicotinamide); and Structure 11, wherein $R_1$-$R_4$ is H and X is $CONH_2$ (isonicotinamide).

9. The compound of claim 1, wherein the compound is a fluoronicotinamide.

10. The compound of claim 1, wherein the compound is 2-fluoronicotinamide.

11. The compound of claim 1, wherein the compound is isonicotinamide.

12. The compound of claim 1, wherein the pharmaceutically acceptable excipient further comprises a second compound of claim 1.

13. A method of inhibiting base exchange more than deacetylation of an acetylated peptide by a SIR2 enzyme, the method comprising

combining the compound of any one of claims 1-12 with the SIR2 enzyme, $NAD^+$ and the acetylated peptide.

14. The method of claim 13, wherein the SIR2 enzyme is derived from a prokaryote or an archaea.

15. The method of claim 13, wherein the SIR2 enzyme is derived from a eukaryote.

16. The method of claim 15, wherein the eukaryote is a mammal.

17. The method of claim 16, wherein the mammalian SIR2 enzyme is a SIR2α.

18. The method of claim 16, wherein the mammal is a human.

19. The method of claim 18, wherein the human SIR2 enzyme is selected from the group consisting of SIR2A, SIRT3, SIRT2p, SIRT1p, SIRT1, SIRT2, SIRT3, SIRT4, SIRT5, SIRT6 and SIRT7.

20. The method of claim 13, wherein the SIR2 enzyme, $NAD^+$ and the acetylated peptide are combined with the compound in a reaction mixture outside of a living cell.

21. The method of claim 13, wherein the SIR2 enzyme is in a living cell.

22. The method of claim 21, wherein the living cell is a eukaryotic cell.

23. The method of claim 21, wherein the living cell is a mammalian cell.

24. The method of claim 23, wherein the mammalian cell is in a living mammal.

25. The method of claim 24, wherein the mammal is a mouse.

26. The method of claim 24, wherein the mammal is a human.

27. A method of increasing protein deacetylation by a SIR2 enzyme in a living cell, the method comprising combining the cell with the compound of any one of claims 1-12.

28. The method of claim 27, wherein the cell is an archaeal cell or a prokaryotic cell.

29. The method of claim 27, wherein the cell is a eukaryotic cell.

30. The method of claim 29, wherein the eukaryotic cell is a mammalian cell.

31. The method of claim 30, wherein the mammalian cell is a mouse cell.

32. The method of claim 30, wherein the mammalian cell is a human cell.

33. The methods of claim 27, wherein the cell is in culture.

34. The method of claim 27, wherein the cell is part of a living organism.

35. A method of increasing deacetylation activity of a SIR2 enzyme, the method comprising combining the compound of any one of claims 1-12 with the SIR2 enzyme, $NAD^+$ and an acetylated peptide substrate of the SIR2.

36. The method of claim 35, wherein the SIR2 enzyme is derived from a prokaryote or an archaea.

37. The method of claim 35, wherein the SIR2 enzyme is derived from a eukaryote.

38. The method of claim 37, wherein the eukaryote is a mammal.

39. The method of claim 38, wherein the mammalian SIR2 enzyme is a SIR2α.

40. The method of claim 38, wherein the mammal is a human.

41. The method of claim 40, wherein the human SIR2 enzyme is selected from the group consisting of SIR2A, SIRT3, SIRT2p, SIRT1p, SIRT1, SIRT2, SIRT3, SIRT4, SIRT5, SIRT6 and SIRT7.

42. The method of claim 35, wherein the SIR2 enzyme, $NAD^+$ and the acetylated peptide are combined in a reaction mixture outside of a living cell.

43. The method of claim 35, wherein the SIR2 enzyme is in a living cell.

44. The method of claim 43, wherein the cell is part of a living organism.

45. A method of inhibiting base exchange more than deacetylation of an acetylated peptide by a SIR2 enzyme, the method comprising displacing nicotinamide from a SIR2 enzymatic site using the compound of any one of claims 1-12.

46. A method of screening a test compound for the ability to increase SIR2 deacctylation activity, the method comprising

combining the test compound with the SIR2 enzyme, $NAD^+$ and an acetylated peptide substrate of SIR2 in a reaction mixture, and determining whether the compound prevents base exchange more than deacetylation.

47. The method of claim 46, wherein the determination is made using a radiolabeled nicotinamide.

48. The method of claim 46, wherein the test compound has one of Structures 1-24 of claim 1.